

Specification Amendments:

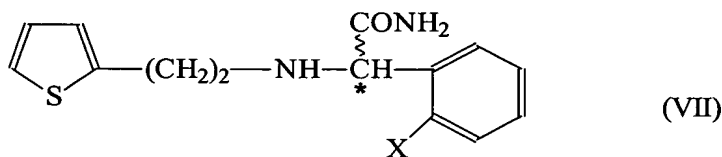
At page 1, following the title and before line 1, please add the following new paragraph:

Cross Reference to Related Applications

This application is a divisional of prior copending application Serial No. 09/830,930, filed June 18, 2001, which is a 35 U.S.C. §371 application of PCT International application No. PCT/HU99/00076 filed November 5, 1999.

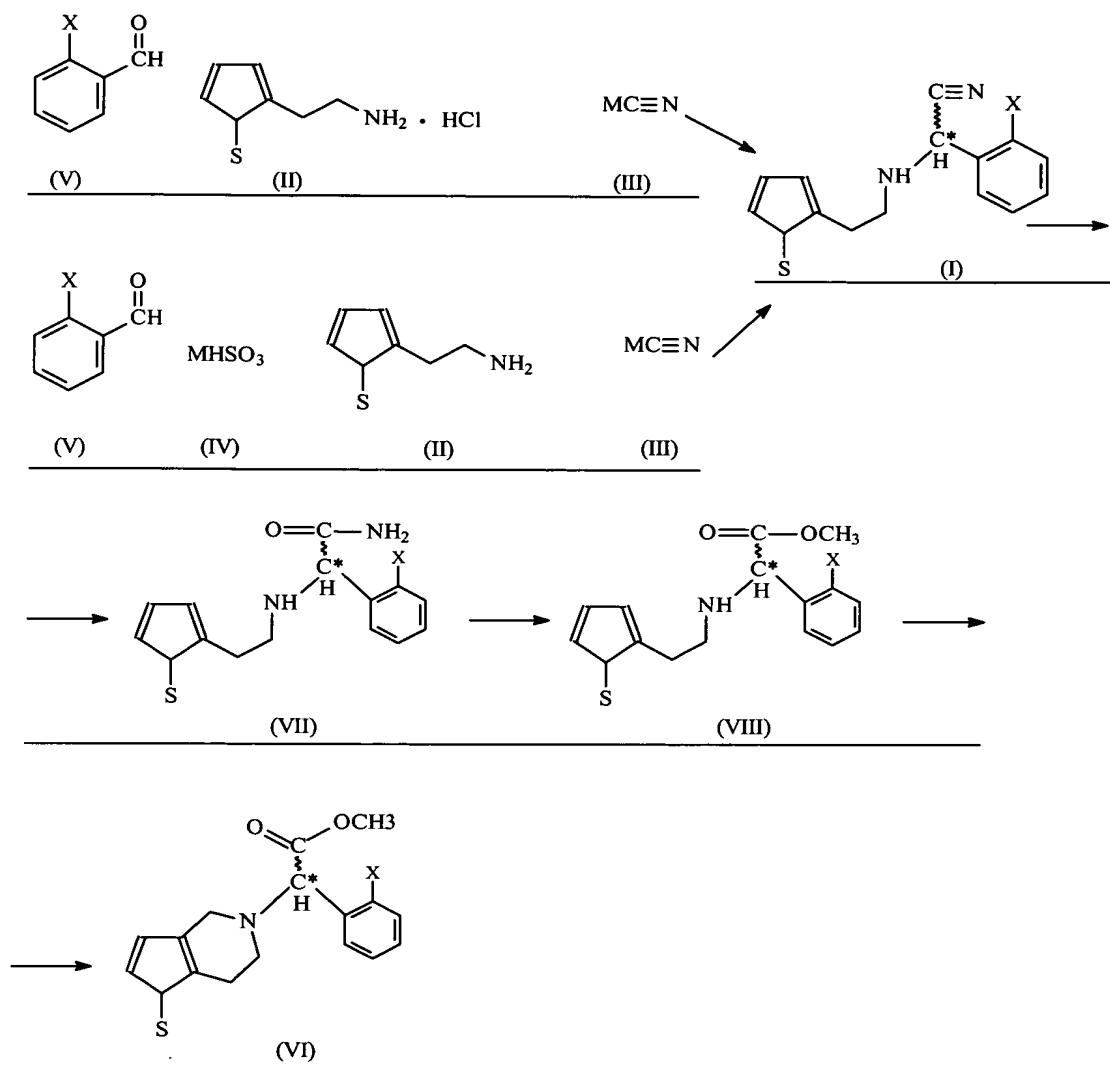
Please replace the paragraph at page 1, lines 1-2, with the following rewritten paragraph:

This invention relates to the novel process for the preparation of the racemic intermediates of ~~general~~ formula (VII) - wherein X ~~represents~~ is halogen atom.



and replace the paragraph at page 1, lines 13 to 18, with the following rewritten paragraph:

PCT applications Nos PCT/HU98/00046, PCT/HU98/00047 and PCT/HU98/00048 (WO 98/51682, WO 98/51681 and WO 98/51689 respectively), which are incorporated herein by reference, ~~whose content through this reference is built into the present application~~— describe the novel synthesis of the compounds of ~~general~~ formula (VI) as shown in the following scheme.



In the course of that synthesis, when the dextrorotatory isomers of the compounds of general formula (VII) are further transformed ~~during the synthesis~~, the levorotatory isomers of the compounds of general formula (VII) form waste and cause considerable loss.

Please replace the paragraphs at page 12, line 21 to page 16, line 21, with the following rewritten paragraphs.

Example [[1.]] 13

29.5 g (0.1 mol) of R-(-)-[2-(2-thienyl)ethylamino](2-chlorophenyl)acetamide is dissolved at 60°C in 120 ml of i-propanol, to the solution 0.8 g (0.02 mol) of sodium

hydroxide is added. The mixture is stirred at 60°C for 20 minutes then it is neutralised with 1.2 ml of acetic acid and concentrated in vacuo to half of its volume. The solution thus obtained is diluted with 200 ml of water, the resulting crystalline product is filtered off, washed with water and dried.

Product: racemic [2-(2-thienyl)ethylamino](2-chlorophenyl)acetamide, weight: 28,6 g (97%), mp: 90-92°C.

IR (KBr), cm^{-1} : 3258, 2862, 1685, 1474, 1445, 1430, 1403, 1387, 1301, 1273, 1247, 1113, 1083, 1049, 1034, 938, 814, 752, 699, 602;

Example [[2.]] 14

29,5 g (0,1 mol) R-(-)-[2-(2-thienyl)ethylamino](2-chlorophenyl)acetamide is dissolved at 60°C in 120 ml of ethanol, to the solution 0.56 g (0.01 mol) of potassium hydroxide is added. The mixture is stirred at 60°C for 30 minutes, then it is neutralized with 0.6 ml of acetic acid and concentrated in vacuo to half of its volume. The solution thus obtained is diluted with 200 ml of water, the resulting crystalline product is filtered off, washed with water and dried.

Product: 28,6 g (97%), mp: 90-92°C.

The product is identical with that of the above Example [[1]] 13.

Example [[3.]] 15

29,5 g (0,1 mol) R-(-)-[2-(2-thienyl)ethylamino](2-chlorophenyl)acetamide is dissolved at 60°C in 120 ml of ethanol, to the solution 2.1 g (0.03 mol) of sodium ethylate is added. The mixture is stirred at 60°C for 30 minutes, then it is neutralized at 40-50°C with 1.8 ml of acetic acid and concentrated in vacuo to half of its volume. The solution thus obtained is diluted with 200 ml of water, the precipitated crystalline product is filtered off, washed with water and dried.

Product: 28 g (95%), mp: 90-92°C.

The product is identical with that of the above Example [[1]] 13.

Example [[4.]] 16

44,5 g (0,1 mol) of R-(-)-[2-(2-thienyl)ethylamino](2-chlorophenyl)acetamide L(+)-tartarate is suspended in 250 ml of i-propanol. To the mixture 10 g (0.25 mol) of sodium

hydroxide is added, it is stirred at 60°C for 30 minutes, then it is neutralized at 40-50°C with 3 ml of acetic acid. The main bulk of the solvent is distilled off in vacuo, the residue is diluted with 300 ml of water, the precipitated crystalline product is filtered off, washed with water and dried.

Product: 28,6 g (97%), mp: 90-92°C.

The product is identical with that of the above Example **[[1]] 13**.

Example **[[5.]] 17**

The procedure as described in Example **[[4]] 16** is followed, but after the end of the reaction and neutralization with acetic acid the resulting L(+) tartaric acid di-sodium salt and sodium acetate are removed by filtration at 60°C. The filtrate is then evaporated in vacuo, giving the product of the same amount and quality as described in Example **[[4]] 16**.

Example **[[6.]] 18**

44.5 g (0.1 mol) of R-(-)-[2-(2-thienyl)ethylamino](2-chlorophenyl)acetamide L(+)-tartarate is suspended in 120 ml of ethanol, to it is added the solution of 20 g (0.5 mol) of sodium hydroxide in 120 ml of water. The mixture is stirred at 50°C for 1 hour, the pH is then adjusted to 6.5 by the addition of 10 % aqueous hydrochloric acid solution and cooled to room temperature. The resulting crystalline product is filtered off, washed with water and dried.

Product: 26,5 g (90%).

The product is identical with that of the above Example **[[1]] 13**.

Example **[[7.]] 19**

44.5 g (0.1 mol) of R-(-)-[2-(2-thienyl)ethylamino](2-chlorophenyl)acetamide L(+)-tartarate is suspended in 600 ml of benzene, to it are added 28 g (0.5 mol) of potassium hydroxide, 72 ml of water and 3 g of tetrabutylammonium bromide. The resulting two-phase mixture is heated under reflux for 1 hour, then, after cooling it to room temperature, it is diluted with 500 ml of water. The phases are separated, the aqueous layer is extracted with 2 x 100 ml of benzene. The united organic phase is washed with 2 x 150 ml of

water, dried over anhydrous sodium sulfate, treated with fuller earth, filtered and evaporated in vacuo. The residue is suspended in 100 ml of ethanol, diluted with 400 ml of water, the crystalline product is filtered off, washed with water and dried.

Product: 28,6 g (97%), op: 90-92°C.

Example ~~[[8.]]~~ 20

33.1 g (0.1 mol) of S-(+)-[2-(2-thienyl)ethylamino](2-chlorophenyl)acetamide hydrochloride is suspended in 120 ml of ethanol, to the mixture 6.2 g (0.11 mol) of potassium hydroxide is added, it is stirred at 60°C for 30 minutes, then it is neutralized at 40-50°C with 0.6 g of acetic acid, and concentrated in vacuo to half of its amount. The solution thus obtained is diluted with 200 ml of water, the resulting crystalline product is filtered off, washed with water and dried.

Product: 28,6 g (97%).

Identification: as described in Example ~~[[1]]~~ 13.

Example ~~[[9.]]~~ 21

44.5 g (0.1 mol) of R-(-)-[2-(2-thienyl)ethylamino](2-chlorophenyl)acetamide L(+)-tartarate is suspended in 220 ml of toluene, to it are added 22.4 g (0.4 mol) of potassium hydroxide, 60 ml of water and 1 g of tetrabutylammonium bromide. The resulting two-phase mixture is stirred at 70° C for 30 minutes, cooled to room temperature, and the phases are separated. The aqueous layer is extracted with 60 ml of toluene, the united organic phases are washed with 2 x 50 ml of water and evaporated in vacuo. The residue is recrystallized from 40 ml of i-propanol. The product is filtered off at 0°C, washed with 40 ml of i-propanol, dried at 40-60°C.

Product: 28,6 g (97%), mp: 90-92°C.

Please delete the paragraph at page 16, lines 22-23, and delete pages 20 and 21 in their entirety.